REMARKS

Upon entry of this amendment claims 3, 9, 10, 18, 26, 52, 55-57, 64-196, and 200-227 are pending. Claims 200-203 and 208-211 are amended to more fully describe the invention; Claims 1-2, 4-8, 11-17, 19-25, 27-51, 53-54, 58-63, 197-199 are canceled, without prejudice or disclaimer; Claims 216-227 are added by this amendment and Claims 64-196 are withdrawn.

Amendments to the Claims

Claims 200-203 and 208-211 are amended to provide correct IUPAC chemical names (see IUPAC, Commission on Nomenclature of Organic Chemistry. A Guide to IUPAC Nomenclature of Organic Compounds, Blackwell Scientific publications, 1993). The recitations of the three specifically named compounds in the claims (a) manganese(II)dichloro-[(4R, 9R, 14R, 19R)-3, 10, 13, 20, 26-pentaazatricyclo[20.3.1.$0^{4,9}$.$0^{14,19}$]-24-chloro-hexacosa-1(26), 22(23), 24(25)-triene]; (b) manganese(II)dichloro-[(4R, 9R, 14R, 19R)-3, 10, 13, 20, 26-pentaazatricyclo[20.3.1.$0^{4,9}$.$0^{14,19}$]-24-chloro-hexacosa-1(26), 22(23), 24(25)-triene]; and (c) manganese(II)dichloro-[(4R, 9R, 14R, 19R)-3, 10, 13, 20, 26-pentaazatricyclo[20.3.1.$0^{4,9}$.$0^{14,19}$]-24-thioethylamine-hexacosa-1(26), 22(23), 24(25)-triene] as amended are both self consistent and consistent with the drawings of the compounds found in Exampes 2, 4 and 5 of the instant application. Thus, the recitation of "pentaazatricyclo" describes the compounds as tricyclic having three rings with the numeric ring size indicators being given in the brackets as 20, 3 and 1 and secondary bridges indicated between positions 4 and 9 and positions 14 and 19. Further, the recitation of the "triene" component is indicated as being comprised of double bonds between positions 1 and 26, positions 22 and 23 and positions 24 and 25 as is apparent from the drawings at the bottom of page 75, the top of page 84 and the top of page 85. Thus, no new matter has been added.

New Claims

Support for the new Claims 216-227 can be found at least in the Claim 60 and Claims 55-57 as originally filed and in the specification as originally filed, on page 9, lines 21-27, page 17, lines 12-19, page 66, line 18 through page 68 line 17 and in Example 20, page 107, line 25 through page 108, line 2. No new matter has been added.

Rejection under 35 U.S.C. § 103(a)

Claims 2-63 and 197 stand rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 6,774,278 to Ragheb et al. ('278), in view of U.S. Patent No. 5,696,109 to Malfroy-Camine et al. ('109) and U.S. Patent No. 5,837,752 to Shastri et al. ('752) and further in view of either Puoyani et al. or Sakurai et al. Applicants respectfully traverse this rejection with respect to the claims currently pending for examination, i.e. Claims 3, 52 and 216 as well as claims that depend therefrom, and request reconsideration and withdrawal of this rejection because none of the

references disclose or suggest the subject matter as recited in the claims. In particular, none of the cited references disclose or suggest pentaazacyclopentadecane compounds nor do any of the cited references disclose or suggest such compounds covalently bound to the surface of a biomaterial or in a copolymer with a biomaterial monomer or in an admixture with a biomaterial.

The '278 patent discloses a medical device for the controlled release of an agent, drug or bioactive material and a list of categories of bioactive materials is provided including free radical scavengers (Col. 3, lns. 14-15; Col. 3, ln. 60 through Col. 4, ln. 10). As recognized by the U.S.P.T.O., however, this reference "is silent to the particular species of the genus of free radical scavengers and antioxidants." Indeed this reference provides no teaching or suggestion whatsoever of pentaazacyclopentadecane compounds. Further, this reference provides no teaching or suggestion of a pentaazacyclopentadecane compound covalently bound to the surface of a biomaterial as recited in Claim 3 or of a copolymer of a pentaazacyclopentadecane compound and a biomaterial monomer as recited in Claim 52 or an admixture of a pentaazacyclopentadecane compound and a biomaterial as recited in Claim 216.

The '109 patent discloses salen-transition metal complexes (see for example Col. 6, lines 43-47). However, this reference provides no teaching or suggestion of a pentaazacyclopentadecane compound or a pentaazacyclopentadecane compound covalently bound to the surface of a biomaterial as recited in Claim 3 or of a copolymer of a pentaazacyclopentadecane compound and a biomaterial monomer as recited in Claim 52 or an admixture of a pentaazacyclopentadecane compound and a biomaterial as recited in Claim 216.

The '752 patent discloses compositions useful as bone cements and tissue implants (Col. 3, lns 14-17 and 21-24). However, this reference provides no teaching or suggestion of a pentaazacyclopentadecane compound or a pentaazacyclopentadecane compound covalently bound to the surface of a biomaterial as recited in Claim 3 or of a copolymer of a pentaazacyclopentadecane compound and a biomaterial monomer as recited in Claim 52 or an admixture of a pentaazacyclopentadecane compound and a biomaterial as recited in Claim 216.

Sakurai et al. discloses the conjugation of proteinaceous superoxide dismutase (SOD) from bovine erythrocytes with sodium hyaluronate by coupling amino groups of SOD with carboxyl groups in the hyaluronate (See Abstract). This reference, however, teaches the conjugation of the proteinaceous SOD with hyaluronate in order to improve biocompatibility and ovecome the limitation of using proteinaceous SOD clinically resulting from rapid clearance from the circulation and induced immune reaction when injected *in vivo* (see page 723, Col. 1, lines 9-12 and Col. 2, line 18). But the pentaazacyclopentadecane compounds recited in Claims 3, 52 and 216 are not proteins at all and one skilled in the art would not expect the same biocompatibility problems associated with a protein to be associated with the

pentaazacyclopentadecane compounds. Further, there is no disclosure or suggestion whatsoever of the non-proteinaceous pentaazacyclopentadecane compounds of the present invention in the Sakurai et al. reference. Moreover, the protein-hyaluronate conjugate disclosed in Sakurai et al. was in the form of a white powder that dissolved to form a solution (see page 723, Col. 1, lines 29-30; Col. 2, lines 13-16) and there is no disclosure or suggestion of a pentaazacyclopentadecane compound covalently bound to the surface of a biomaterial as recited in Claim 3 or of a copolymer of a pentaazacyclopentadecane compound and a biomaterial monomer as recited in Claim 52 or of an admixture of a pentaazacyclopentadecane compound and a biomaterial as recited in Claim 216.

Contrary to what was stated by the U.S.P.T.O. the Pouyani et al. does not disclose the conjugating of superoxide dismutase to hyaluronic acid at all, but instead, this reference discloses the covalent attachment of hyaluronic acid to ibuprofin and to hydrocortisone (see page 344, line 8 through page 345, line 8). This reference, however, fails to disclose or suggest the pentaazacyclopentadecane compounds of the present invention or a pentaazacyclopentadecane compound covalently bound to the surface of a biomaterial as recited in Claim 3 or of a copolymer of a pentaazacyclopentadecane compound and a biomaterial monomer as recited in Claim 52 or an admixture of a pentaazacyclopentadecane compound and a biomaterial as recited in Claim 216.

Thus, none of the references cited by the U.S.P.T.O. disclose the subject matter recited in the claims as amended and withdrawal of the rejection with respect to the currently pending claims is respectfully requested.

Moreover, Applicants have further described the novelty and nonobviousness of the invention in a literature article published by Applicants after the filing date of the instant application (see Udipi et al., Modification of inflammatory response to implanted biomedical materials *in vivo* by surface bound superoxide dismutase mimics, *J. Biomed Mater Res 51(4)*:549-60, 2000). In this article, Applicants report on a surface conjugation of superoxide dismutase mimic (SODm) to biomedical materials (Abstract, page 549, Col.1, lines 12-16) as well as a melt processing in polypropylene that produces an admixture (page 559, Col. 1, lines 27-30) as reported more fully in the instant application (*see* Examples 7-13 and 16-20). Implantation of the modified biomaterials produces both acute and chronic anti-inflammatory effects (Abstract, Col. 1, line16 through Col. 2, line 2; *see also* Example 21 of the instant application). Applicants report that "[t]hese results are, to our knowledge, the first description of a general anti-inflammatory surface treatment for biomedical materials." (page 557, col. 2, lines 3-6 from bottom). Moreover, Applicants report that the SODm remains firmly bound during 28 days *in vivo* showing an antiinflammatory effect that is described as striking (Abstract, Col. 2,

lines 2-8; page 559, lines 1-3 from bottom; *see also* Example 21 of the instant application). This ability to remain firmly bound to the biomaterial and to continue to exert superoxide dismutase activity for 28 days while being bound to the biomaterial was unknown and could not have been predicted prior to Applicants' successful discovery. Hence, Applicants' invention is both novel and non-obvious over what was known in the art at the time the invention was made.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of rejections of the claims. It is believed that the claims as currently presented are in a condition for allowance and such favorable action is respectfully requested. If any questions arise or if any issues remain to be resolved, it is requested that the Examiner contact the undersigned attorney.

Respectfully submitted,

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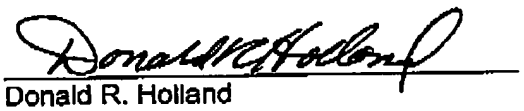
By: 

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